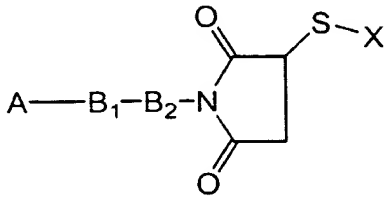
WHAT IS CLAIMED IS:

1. A water-soluble compound of the formula



wherein:

A is a water-insoluble drug;

B_1 and B_2 together are a spacer moiety; and

X is a polar moiety;

or a pharmaceutically acceptable salt of said compound.

2. The compound of claim 1, wherein

B_1 is selected from the group consisting of a methylenyl, an amido, -N=, an amino, and a thiol maleimido, and

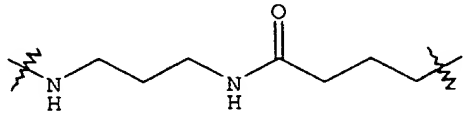
B_2 is selected from the group consisting of a C_1-C_{19} alkylamido, a C_1-C_{19} alkyl, a C_2-C_{19} alkenyl, a C_2-C_{19} alkynyl, a C_1-C_{19} hydroxyalkyl, a C_1-C_{19} alkyl carbamoyl, a C_1-C_{19} alkylcarbonyl, and an aralkyl, any of which can be further substituted with one or more substitutents, which can be the same or different, selected from the group consisting of a nitro, a halo, an azido, a hydroxy, an amido, and an amino group.

3. The compound of claim 2, wherein

B_2 is selected from the group consisting of a C_1-C_7 alkylamido, a C_1-C_7 alkyl, a C_2-C_7 alkenyl, a C_2-C_7 alkynyl, a C_1-C_7 hydroxyalkyl, a C_1-C_7 alkyl carbamoyl, a C_1-C_7

alkylcarbonyl, and an aralkyl, any of which can be further substituted with one or more substituents, which can be the same or different, selected from the group consisting of a nitro, a halo, an azido, a hydroxy, an amido and an amino group.

4. The compound of claim 3, wherein said spacer moiety has the structure



5. The compound of any of claims 1-4, wherein said polar moiety is an amino acid, a peptide, a polypeptide, or a protein.

6. The compound of claim 5, wherein said polar moiety is L-cysteine.

7. The compound of any of claims 1-4, wherein said polar moiety is ionic at neutral pH.

8. The compound of claim 7, wherein said compound is zwitterionic at neutral pH.

9. The compound of any of claims 1-8, wherein said water-insoluble drug is an anticancer drug.

10. The compound of any of claims 1-8, wherein said water-insoluble drug is a macrolide or an ansamacrolide.

11. The compound of any of claims 1-8, wherein said drug is geldanamycin or a derivative thereof.

12. The compound of any of claims 1-8, wherein said drug is an anti-hypertension drug.

13. The compound of any of claims 1-8, wherein said water-insoluble drug is an antibiotic drug.

14. A pharmaceutical composition comprising a pharmaceutically acceptable carrier and a compound of any of claims 1-13.

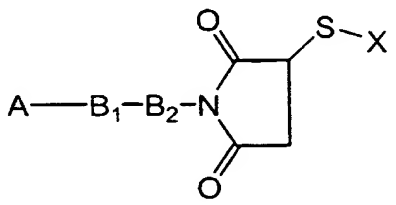
15. A method of treating cancer in a mammal, which method comprises administering to a mammal having cancer an anticancer effective amount of a compound of any of claims 1-11.

16. A method of rendering soluble in water a water-insoluble drug, which method comprises:

(i) providing a water-insoluble drug comprising a side-chain that can react with a bifunctional linking molecule;

(ii) contacting said water-insoluble drug with said bifunctional linking molecule to obtain a first derivative comprising a maleimide side-chain;

(iii) contacting said first derivative with a thio containing polar moiety (X-SH) to obtain a water-soluble compound of the formula



wherein:

A is a water-insoluble drug;

B_1 and B_2 together are a spacer moiety; and

X is a polar moiety;

or a pharmaceutically acceptable salt of said compound.

17. The method of claim 16, wherein

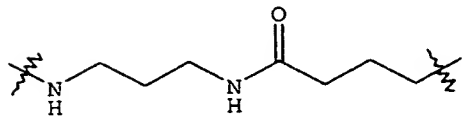
B_1 is selected from the group consisting of methylenyl, an amido, -N=, an amino, and a thiol maleimido, and

B_2 is selected from the group consisting of a C_1-C_{19} alkylamido, a C_1-C_{19} alkyl, a C_2-C_{19} alkenyl, a C_2-C_{19} alkynyl, a C_1-C_{19} hydroxyalkyl, a C_1-C_{19} alkyl carbamoyl, a C_1-C_{19} alkylcarbonyl, and an aralkyl, any of which can be further substituted with one or more substituents, which can be the same or different, selected from the group consisting of a nitro, a halo, an azido, a hydroxy, an amido and an amino group.

18. The method of claim 17, wherein

B_2 is selected from the group consisting of a C_1-C_7 alkylamido, a C_1-C_7 alkyl, a C_2-C_7 alkenyl, a C_2-C_7 alkynyl, a C_1-C_7 hydroxyalkyl, a C_1-C_7 alkyl carbamoyl, a C_1-C_7 alkylcarbonyl, and an aralkyl, any of which can be further substituted with one or more substituents, which can be the same or different, selected from the group consisting of a nitro, a halo, an azido, a hydroxy, an amido, and an amino group.

19. The method of claim 18, wherein said spacer moiety has the structure



20. The method of any of claims 16-19, wherein step (i) comprises contacting a water-insoluble drug with a modifying agent to provide a water-insoluble drug comprising a side-chain that can react with a bifunctional linking molecule.

21. The method of claim 20, wherein said water-insoluble drug comprises a methoxyaryl moiety that can react with said modifying agent, and said modifying agent comprises a primary amine, whereupon reacting said water-insoluble drug with said modifying agent, a demethoxy derivative of said water-insoluble drug comprising a portion of said modifying agent as a side chain is provided and wherein said portion of said modifying agent can react with said bifunctional linking molecule.

22. The method of claim 20 or 21, wherein said modifying agent is a diaminoalkane.

23. The method of claim 22, wherein said diaminoalkane is 1,3-diaminopropane or 1,4-diaminobutane.

24. The method of any of claims 16-23, wherein said thio containing polar moiety is a polypeptide or a protein.

25. The method of any of claims 16-24, wherein said thio containing polar moiety is an amino acid.

26. The method of claim 25, wherein said amino acid is cysteine.

27. The method of any of claims 16-26, wherein said water-insoluble drug is an anticancer drug.

28. The method of any of claims 16-27, wherein said water-insoluble drug is an antibiotic drug.

29. The method of any of claims 16-27, wherein said water-insoluble drug is an anti-hypertension drug.

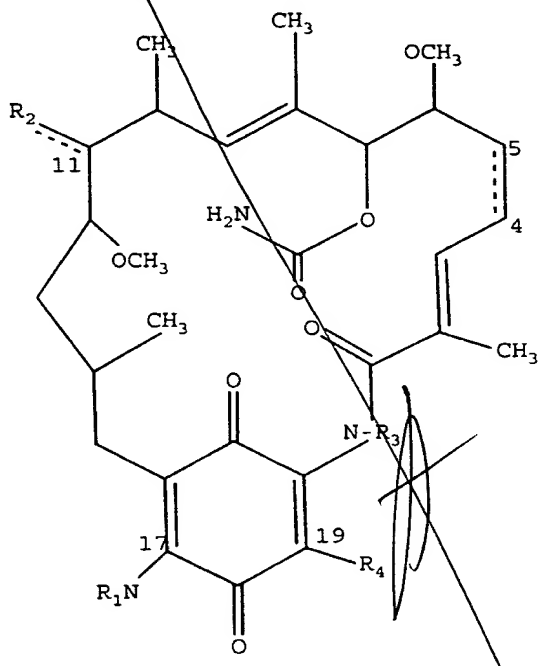
30. The method of any of claims 16-27, wherein said water-insoluble drug is a macrolide or an ansamacrolide.

31. The method of any of claims 16-27, wherein said water-insoluble drug is geldanamycin or a derivative of geldanamycin.

32. The method of any of claims 16-32, wherein said bifunctional linking molecule is selected from the group consisting of N-γ-maleimidobutyryloxysuccinimide ester (GMBS), sulfo-N-γ-maleimidobutyryloxysuccinimide ester (sulfo-GMBS), *m*-maleimidobenzoyl-N-hydroxysuccinimide ester (MBS), *m*-maleimidobenzoyl-N-hydroxysulfosuccinimide ester (sulfo-MBS), succinimidyl4-[*p*-maleimidophenyl]butyrate (SMPB), sulfosuccinimidyl4-[*p*-maleimidophenyl]butyrate (sulfo-SMPB), succinimidyl 4-[N-maleimidomethyl]cyclohexane-1-carboxylate (SMCC), sulfosuccinimidyl 4-[N-maleimidomethyl]cyclohexane-1-carboxylate (sulfo-SMCC), 4-[N-maleimidomethyl]-cyclohexane-1-carboxylhydrazide-HCl (M2C2H), and 4-[4-maleimidophenyl]-butyric acid hydrazide-HCl (MPBH).

33. The method of claim 32, wherein said bifunctional linking molecule is sulfo-N-γ-maleimidobutyryloxysuccinimide ester (sulfo-GMBS).

34. A water-soluble compound of the formula



or a pharmaceutically acceptable salt thereof, wherein:

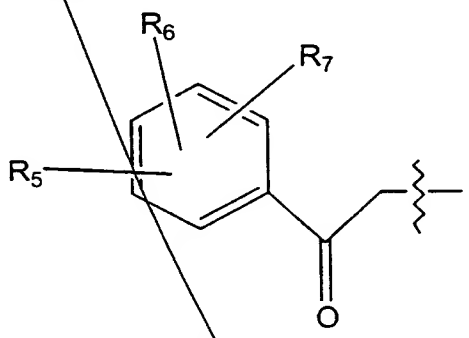
R_1 is an ionic moiety bound to the carbon at position 17 via a nitrogen atom,

R_2 is a halo or an $-OR_8$ when there is a single bond between R_2 and the carbon at position 11, wherein R_8 is selected from the group consisting of hydrogen, a C_1-C_8 alkylamido, a C_1-C_8 alkyl, a C_2-C_8 alkenyl, a C_2-C_8 alkynyl, a C_1-C_8 hydroxyalkyl, a C_1-C_8 alkyl carbamoyl, a C_1-C_8 alkylcarbonyl, and an aralkyl, any of which R_8 groups can be further substituted with one or more substituents, which can be the same or different, selected from the

group consisting of a nitro, a halo, an azido, a hydroxy, an amido and an amino groups, or

R_2 is oxo (=O) or oximino (=NOH) when there is a double bond between R_2 and the carbon at position 11,

R_3 is selected from the group consisting of hydrogen and a group of the formula



wherein R_5, R_6, and R_7 are each independently selected from the group consisting of hydrogen, a halo, an azido, a nitro, a C_1-C_8 alkyl, a C_1-C_8 alkoxy, an aryl, a cyano, and an $NR_{10}R_{11}R_{12}$, wherein R_{10}, R_{11}, and R_{12} are each independently selected from the group consisting of hydrogen and a C_1-C_3 alkyl,

R_4 is selected from the group consisting of hydrogen, a halo, a C_1-C_8 alkylamino, and a C_1-C_8 dialkylamino, and

the bond between the carbons at positions 4 and 5 can be a single bond or a double bond.

35. The compound of claim 34, wherein R_1 is an aliphatic moiety which optionally comprises an aryl ring, wherein said aliphatic moiety is substituted by one or more charged moieties, which can be the same or different, selected from the group consisting of carbamate, carbonate, carboxylate, phosphamate, phosphate, phosphonate, pyrophosphate, triphosphate, sulfamate, sulfate, sulfonate, a C_1-C_8 monoalkylamine that

is protonated at neutral pH, a C_1-C_4 dialkylamine that is protonated at neutral pH, and a C_1-C_4 trialkylammonium, such that R_1 is charged at neutral pH.

36. The compound of claim 35, wherein R_1 is selected from the group consisting of a C_1-C_{19} alkylamido, a C_1-C_{19} alkyl, a C_2-C_{19} alkenyl, a C_2-C_{19} alkynyl, a C_1-C_{19} hydroxyalkyl, a C_1-C_{19} alkyl carbamoyl, a C_1-C_{19} alkylcarbonyl, and an aralkyl, any of which can be further substituted with one or more substituents, which can be the same or different, selected from the group consisting of a nitro, a halo, an azido, a hydroxy, an amido, and an amino group.

37. The compound of claim 36, wherein R_1 is selected from the group consisting of a C_1-C_7 alkylamido, a C_1-C_7 alkyl, a C_2-C_7 alkenyl, a C_2-C_7 alkynyl, a C_1-C_7 hydroxyalkyl, a C_1-C_7 alkyl carbamoyl, a C_1-C_7 alkylcarbonyl, and a monocarbocyclic aralkyl any of which can be further substituted with one or more substituents, which can be the same or different, selected from the group consisting of a nitro, a halo, an azido, a hydroxy, an amido, and an amino group..

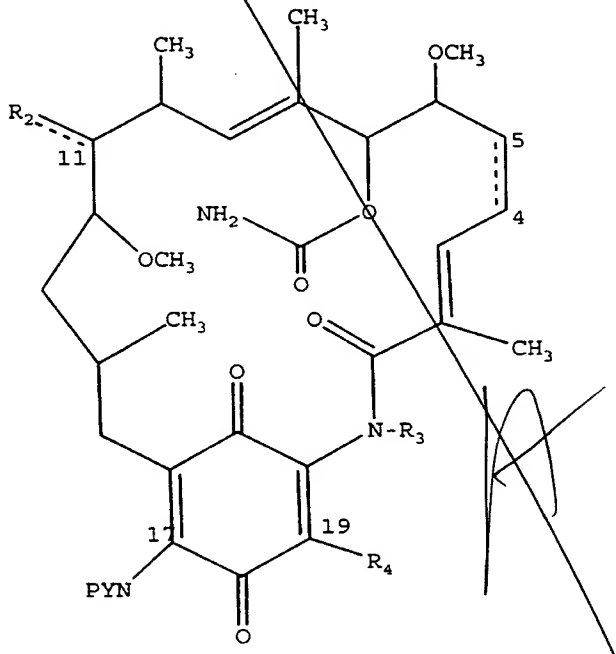
38. The compound of claim 36 or 37, wherein said aliphatic moiety comprises a moiety selected from the group consisting of a nucleoside, a saccharide, and an amino acid.

39. The compound of claim 36 or 37, wherein said aliphatic moiety comprises an amino acid.

40. The compound of claim 39, wherein said amino acid is lysine.

41. The compound of any of claims 34-40, wherein R_1 is zwitterionic at neutral pH.

42. A water-soluble compound of the formula



or a pharmaceutically acceptable salt thereof, wherein:

Y is a spacer group,

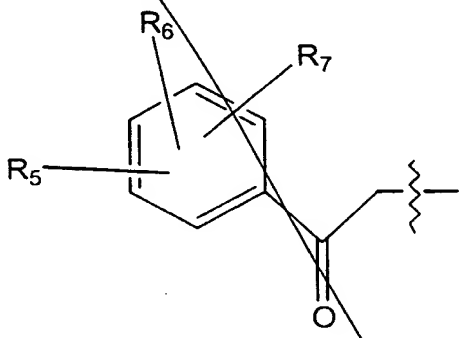
P is a polypeptide or a protein that selectively binds to the surface of a mammalian cell,

R_2 is a halo or an $-OR_8$ when there is a single bond between R_2 and the carbon at position 11, wherein R_8 is selected from the group consisting of hydrogen, a C_1-C_8 alkylamido, a C_1-C_8 alkyl, a C_2-C_8 alkenyl, a C_2-C_8 alkynyl, a C_1-C_8 hydroxyalkyl, a C_1-C_8 alkyl carbamoyl, a C_1-C_8 alkylcarbonyl, and an aralkyl, any of which R_8 groups can

be further substituted with one or more substituents, which can be the same or different, selected from the group consisting of a nitro, a halo, an azido, a hydroxy, an amido, and an amino group, or

R_2 is oxo (=O) or oximino (=NOH) when there is a double bond between R_2 and the carbon at position 11,

R_3 is selected from the group consisting of hydrogen and a group of the formula



wherein R_5, R_6, and R_7 are each independently selected from the group consisting of hydrogen, a halo, an azido, a nitro, a C_1-C_8 alkyl, a C_1-C_8 alkoxy, an aryl, a cyano, and an $NR_{10}R_{11}R_{12}$, wherein R_{10} , R_{11}, and R_{12} are each independently selected from the group consisting of hydrogen and a C_1-C_3 alkyl,

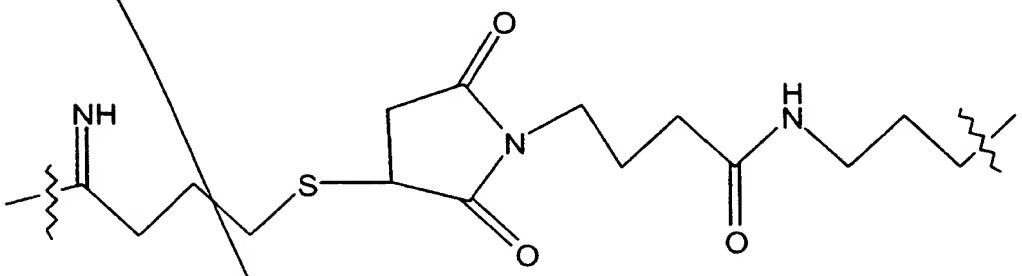
R_4 is selected from the group consisting of hydrogen, a halo, a C_1-C_8 alkylamino, and a C_1-C_8 dialkylamino, and

the bond between the carbons at positions 4 and 5 can be a single bond or a double bond.

43. The compound of claim 42, wherein Y comprises a thio ether.

44. The compound of claim 43, wherein P comprises a lysine and Y is bonded to P via said lysine.

45. The compound of claim 43 or 44, wherein Y is



46. The compound of any of claims 41-46, wherein said protein or polypeptide binds to an antigen.

47. The compound of claim 46, wherein said protein or polypeptide is an antibody, or an antigenically reactive fragment thereof, wherein said antibody is optionally humanized.

48. The compound of claim 47, wherein said protein is herceptin or e21.

49. The compound of claim 47, wherein said antibody is selected from the group consisting of huB4, BR96, and Zenapax.

50. The compound of claim 47, wherein said antibody is C225.

51. The compound of claim 47, wherein said protein is selected from the group comprising a diabody, a Fab, a Fab'_2, a single-chain antibody, and a single-chain Fab.

52. The compound of claim 41-46, wherein said polypeptide or protein is a secreted by a cell.

53. The compound of claim 52, wherein said polypeptide or protein is an interleukin.

54. The compound of claim 53, wherein said interleukin is interleukin-2.

55. The compound of claim 52, wherein said protein is a growth factor.

56. The compound of claim 52, wherein said polypeptide or protein is vascular endothelial growth factor or epidermal growth factor.

57. The compound of claim 52, wherein said polypeptide or protein is heregulin.

58. The compound of any of claims 42-57, wherein said polypeptide or protein binds to a receptor of a cell of a mammal, and wherein said compound is internalized into said cell of a mammal.

59. A method of treating cancer in a mammal, which method comprises administering to a mammal having cancer an anticancer effective amount of a compound comprising a polypeptide or protein covalently bonded to 17-demethoxy-17-amino-geldanamycin or a derivative thereof, wherein said polypeptide or protein binds to the surface of a cancer cell.

60. The method of claim 59, wherein said polypeptide or protein is bonded to said 17-demethoxy-17-

amino-geldanamycin or a derivative thereof via a spacer moiety comprising a thio ether.

61. The method of claim 59 or 60 wherein said polypeptide or protein binds to an antigen.

62. The method of any of claims 59-61, wherein said compound is internalized by said cancer cell.